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ORIGINAL RESEARCH

Impact of exacerbations on health care cost and resource utilization in chronic obstructive pulmonary disease patients with chronic bronchitis from a predominantly Medicare population

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http://dx.doi.org/10.2147/COPD.S36997

Background: Exacerbations of chronic obstructive pulmonary disease (COPD) lead to significant increases in resource utilization and cost to the health care system. COPD patients with chronic bronchitis and a history of exacerbations pose an additional burden to the system. This study examined health care utilization and cost among these patients.

Methods: For this retrospective analysis, data were extracted from a large national health plan with a predominantly Medicare population. This study involved patients who were aged 40–89 years, had been enrolled continuously for 24 months or more, had at least two separate insurance claims for COPD with chronic bronchitis (International Classification of Diseases, Ninth Revision, Clinical Modification code 491.xx), and had pharmacy claims for COPD maintenance medications between January 1, 2007, and March 31, 2009. Two years of data were examined for each patient; the index date was defined as the first occurrence of COPD. Baseline characteristics were obtained from the first year of data, with health outcomes tracked in the second year. Severe exacerbation was defined by COPD-related hospitalization or death; moderate exacerbation was defined by oral or parenteral corticosteroid use. Adjusted numbers of exacerbations and COPD-related costs per patient were estimated controlling for demographic and clinical characteristics.

Results: The final study sample involved 8554 patients; mean age was 70.1 ± 8.6 years and 49.8% of the overall population had exacerbation, 13.9% had a severe exacerbation only, 29.1% had a moderate exacerbation only, and 6.8% had both a severe and moderate exacerbation. COPD-related mean annual costs were \$4069 (all figures given in US dollars) for the overall population and \$6381 for patients with two or more exacerbations. All-cause health care costs were \$18,976 for the overall population and \$23,901 for patients with history of two or more exacerbations. Severity of exacerbations, presence of cardiovascular disease, diabetes, and long-term oxygen use were associated with higher adjusted costs.

Conclusions: The results indicate that despite treatment with maintenance medications, COPD patients continue to have exacerbations resulting in higher costs. New medications and disease management interventions are warranted to reduce the severity and frequency of exacerbations and the related cost impact of the disease.

Keywords: COPD with chronic bronchitis, moderate exacerbation, severe exacerbation, Medicare patients

Introduction

Chronic obstructive pulmonary disease (COPD) is a major public health problem because of its high incidence and COPD-related morbidity and mortality.¹ Chronic lower respiratory diseases are the third-leading cause of death in the United States

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International Journal of COPD 2012:7 757–764

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and have both a significant health impact and a significant economic impact on society.² In fact, a diagnosis of COPD was reported for 5.1% of adults in the United States between 2007 and 2009, and the disease was more prevalent in older age groups and in women more than men.³

Patients with COPD have a progressive condition in which airflow is consistently obstructed, making it difficult for these patients to breathe.⁴ These patients may experience an acute worsening of respiratory symptoms such as elevated sputum volume, sputum purulence, and dyspnea, defined as a COPD exacerbation, which is associated with poor outcomes in terms of both morbidity and mortality.⁵ While exacerbations are infrequent in early COPD, they can be life threatening and can occur on average three times a year in patients with moderate to severe COPD.^{4,6}

Exacerbations are associated with disease progression by accelerating reductions in lung function measured by forced expiratory volume in one second (FEV₁).^{5,7} Additionally, the literature suggests that nearly half of all exacerbations remain unreported, which may also have an impact on health status.⁸ An increase in the number of exacerbations experienced by a patient may have a deleterious effect on the patient's health-related quality of life¹ and can greatly increase the burden of health-related services and economic costs attributable to this disease.^{9–11}

Acute episodes leading to inpatient care incur the greatest medical costs in patients with COPD.^{10,11} Nationally, the direct cost of COPD in the United States for 2010, as estimated by the National Heart, Lung, and Blood Institute, was \$29.5 billion (all figures given in US dollars), with \$13.2 billion in hospital care costs, \$5.5 billion in physician services, and \$5.8 billion in prescription drugs.¹² As demonstrated by Dalal et al¹³ in a study of commercially insured patients with COPD, direct costs associated with increasing severity of exacerbations resulting in hospitalization significantly drove the cost of health care, regardless of whether or not patients were treated in hospital intensive care units.

While early treatment and recognition of exacerbation symptoms have been shown to improve health outcomes, approximately 50% of exacerbations remain unreported and consequently do not receive adequate treatment.^{8,14,15} Once a treatment regimen has been initiated, management of stable COPD is meant to reduce the number and intensity of exacerbations.^{12,16} Severely ill patients may receive oxygen therapy, but maintenance medications are generally added as the disease progresses and can include short-acting β 2-agonists, long-acting β -agonists (LABAs), long-acting muscarinic antagonists (LAMAs), inhaled

glucocortic osteroids (ICSs), phosphodiesterase-4 inhibitor, or the ophylline. $^{\rm 17}$

Various studies have demonstrated the effectiveness of these COPD medications and their combinations for reducing exacerbations; however, the results have been mixed.^{18–20} Few studies have examined the influence of multiple exacerbations, differing treatment regimens, and population disparities in health care cost and utilization. The current study addresses these gaps through examination of the frequency of moderate and severe exacerbations, and examination of associated health care utilization and costs in detail, of patients with a history of exacerbations diagnosed with COPD and chronic bronchitis in a predominantly Medicare population.

Methods

Data source

De-identified health care claims data from a large national health care company were used for this analysis. Data included administrative claims for more than 3 million members from a fully insured commercial health plan and Medicare Advantage Prescription Drug Plan members. The data included medical claims, pharmacy claims, and eligibility files from the health plan database. Patient privacy was maintained by masking identification in accordance with the Health Insurance Portability and Accountability Act of 1996.

Patient population

Fully insured patients aged between 40 and 89 years at the index date (defined as the first occurrence of COPD) who were enrolled continuously for 24 months or more, who had at least two separate inpatient or outpatient insurance claims for COPD with chronic bronchitis - as identified by the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis code of 491.xx in any diagnosis position – from January 1, 2007, to March 31, 2009, and who had pharmacy claims for COPD maintenance medications were included in the study (Figure 1). Maintenance medications included LABAs, LAMAs, ICSs, and SAMAs and are listed in Table 1. Patients were excluded if they had medical claims for any malignant neoplasm of the lung (ICD-9-CM codes 162.xx and 197.0), asthma (ICD-9-CM code 493.xx) or allergic alveolitis (ICD-9-CM code 495.xx) during the study time period.

Study design

Patients were identified by the first occurrence of COPD with chronic bronchitis (ICD-9-CM code 491.xx), which,

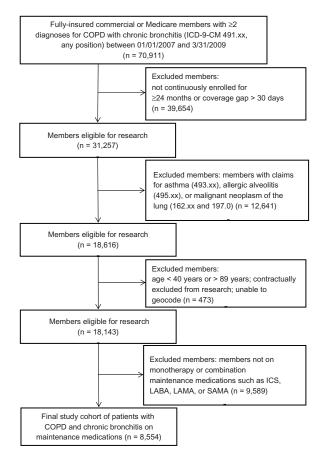


Figure I Selection of study participants: claims data from a large national health plan were used to identify patients diagnosed with chronic obstructive pulmonary disease (COPD) and chronic bronchitis who experienced two or more exacerbations within the study time period.

Note: Exclusion criteria were applied to remove patients with a claims history that did not meet the study requirements.

Abbreviations: ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; ICSs, inhaled glucocorticosteroids; LABAs, long-acting β 2-agonists; LAMAs, long-acting muscarinic antagonists; SAMAs, short-acting muscarinic antagonists.

as mentioned earlier, was defined as the index date. Claims activity for each patient was followed for 2 years after the index date. Year 1 was defined as the 12 months following the index date and was used to gather baseline information and define specific subgroups (patients with one or more exacerbations, those with two or more exacerbations, and those aged 65 years or older); Year 2 (the follow-up year) was defined as the 13–24 months post index and was used to measure outcomes and costs.

The occurrence of severe and moderate exacerbations was determined through claims data and this was used for tracking health care costs and utilization. The definition of a moderate or severe exacerbation was adapted and slightly modified from the method previously described by Yu et al.²¹ A severe exacerbation was defined by COPD-related hospitalization or death (identified by discharge status of "died" or by ICD-9 -CM code 798) within 7 days of a COPD diagnosis (defined by

Table	L	Demographic	and	clinical	characteristics	in	sample
(n = 855)	(4						

Characteristic	Results
Age (years) [mean (SD)]	70.1 (8.6)
Aged 65 years or older [n (%)]	6759 (79.0)
Gender (% female)	50.2
Race/ethnicity [n (%)]	
White	5806 (68.7)
Black	659 (7.8)
Hispanic	466 (5.5)
Other	1515 (17.9)
United States geographic region [n (%)]	
Midwest	2076 (24.3)
Northeast	147 (1.7)
South	5670 (66.5)
West	639 (7.5)
Income level [n (%)] ^a	
Low (≤\$33,541)	2317 (27.1)
Medium (>\$33,541 to <\$52,480)	4195 (49.0)
High (≥\$52,480)	2042 (23.9)
DCI score [mean (SD)] ^b	1.9 (1.8)
Top five comorbidities [n (%)]	
Related COPD diagnoses ^c	1968 (23.0)
Diabetes without complication	1900 (22.2)
Congestive heart failure	1568 (18.3)
Peripheral vascular disease	972 (11.4)
Renal disease	822 (9.6)
Maintenance medications (total) [n (%)] ^d	
LABA alone	360 (4.2)
LAMA alone	3708 (43.4)
Any ICS	8554 (100)
ICS + LABA combination	4472 (52.3)
ICS + LABA + LAMA combination	2130 (24.9)
Other respiratory medications (total) [n (%)]	
SAMA and combinations	4611 (53.9)
Methylxanthines	520 (6.1)
Oral/IV corticosteroids	5289 (61.8)
Antibiotics	7203 (84.2)
Long-term oxygen use	3525 (41.2)
Mean number of total drugs taken for the year [n (SD)]	14.65 (6.9)

Notes: *All figures given in US dollars; ^bthe range for the DCI score was 0–16; ^crelated COPD diagnoses (chronic pulmonary heart disease, COPD and allied conditions other than ICD-9-CM code 491.x, and respiratory conditions due to external agents) are ICD-9-CM codes 416.8, 416.9, 490, 492, 493, 494, 495, 496, 500, 501, 502, 503, 504, 505, 506.4, 508.1, and 508.8; ^dcategories of maintenance medication prescriptions are not mutually exclusive.

Abbreviations: DCI, Deyo-Charlson Comorbidity Index; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; ICS, inhaled glucocorticosteroid; IV, intravenous; LABA, long-acting β 2-agonist; LAMA, long-acting muscarinic antagonist; SAMA, short-acting muscarinic antagonist; SD, standard deviation.

the following ICD-9-CM codes: 490.xx, 491.xx, 492.xx, 494.1, or 496.xx). A moderate exacerbation was defined by oral or parenteral corticosteroid use on the same day or within 7 days of a COPD-related diagnosis claim (as identified by the same ICD-9-CM codes: 490.xx, 491.xx, 492.xx, 494.1, or 496.xx). Allergic alveolitis (495.xx) was excluded from this study's definition of COPD exacerbation.

The Deyo-Charlson adaptation of the Charlson Comorbidity Index (DCI) was used to determine the disease burden for each patient.²² The Deyo adaptation includes 17 diseases that were selected and weighted on the basis of the strength of their association with mortality.

One variable indicating use of long-term oxygen therapy was created for "severity" of disease, based on baseline period treatments consistent with the Global Initiative for Chronic Obstructive Lung Disease guidelines¹⁷ for severe and very severe patients. Very severe patients are recommended long-term oxygen therapy. This variable was used to control for severity in regression analyses.

Race data were available for Medicare patients in the study sample; however, race assignment for commercial health plan members required the use of geocoding at the census tract level to impute race/ethnicity values.

Statistical analysis

All analyses were conducted using SAS (v 9.3; SAS Institute Inc, Cary, NC) and Enterprise Guide (v 4.3; SAS Institute Inc). *P*-values ≤ 0.05 were considered to indicate statistically significant differences. A generalized linear model (GLM), with log link and gamma distribution for the error term, was used to estimate adjusted health care costs, controlling for demographic and clinical characteristics. A GLM is an extension of linear regression models that can handle non-normally distributed data with nonconstant variances.²³ A fitted GLM was used to produce an adjusted mean cost estimate for patients with each type of exacerbation. Independent variables in the models included age, gender, race/ethnicity, geographic region, income level, and comorbidities recorded at baseline. Covariates included whether or not a patient experienced a severe and/or a moderate exacerbation (reference group: no exacerbations), and various types of medication treatment.

Results

The final study sample involved 8554 patients. The demographic and clinical characteristics of the COPD population taking maintenance medications as measured in the identification period (Year 1) are reported in Table 1. The mean age of the population was 70.1, with 79% of patients aged 65 years or older. The population was mainly made up of Medicare health plan members (96.5%), and was split evenly between the genders. The sample consisted predominantly of white members residing in the southern United States, with nearly half (49%) of the sample reporting a medium income level. The medium income level was made up of incomes between \$33,541 and \$52,480 after the sample income was divided into tertiles.

For all patients, the mean DCI score was 1.9 (standard deviation, 1.8; range, 0–16). Among the comorbidities used to calculate the DCI score, the top comorbidity was related COPD diagnoses (23.0%, including chronic pulmonary heart disease, COPD and allied conditions other than 491.x, and respiratory conditions due to external agents). This was closely followed by diabetes without complication and congestive heart failure (22.2% and 18.3%, respectively). Peripheral vascular disease and renal disease were also included in the top five comorbidities (11.4% and 9.6%, respectively).

Among the maintenance medications taken by the patients in this study, 100% of the population had filled one or more prescriptions for ICS, 52.3% for ICS and LABA combination drugs, 43.4% for LAMAs, and 24.9% for triple ICS, LABA, and LAMA combination therapy. These categories were not mutually exclusive – that is, a patient may have been included in more than one category. In addition to COPD maintenance medications, the majority of patients (84.2%) filled one or more prescriptions for antibiotics during the course of the year, 61.8% were treated with oral or parenteral corticosteroids, and 41.2% were receiving long-term oxygen therapy.

The proportion of patients with each type of exacerbation, as well as number of exacerbations during the follow-up year, is provided in Table 2 and is categorized as patients with one or more exacerbations, those with two or more exacerbations, and those aged 65 years or older. Of the overall population on maintenance medications, 49.8% had any type of exacerbation. Within this group, 13.9% had severe exacerbations only, 29.1% had moderate exacerbations only, and 6.8% had both a severe and a moderate exacerbation. The overall population was also stratified into three patient categories: (1) patients with one or more exacerbations during the baseline period, (2) patients with two or more exacerbations during the baseline period, and (3) patients aged 65 years or older. As with maintenance medications, these subgroups were not mutually exclusive. As expected, patients with two or more exacerbations during the baseline period had the highest rate of exacerbations per patient in the follow-up year among the three subgroups, followed by patients with one or more exacerbations (Table 2). The rates of exacerbations per patient per year during the follow-up year for all subgroups were as follows: 1.26 for the subgroup with one or more exacerbations at baseline, 1.77 for the subgroup with two or more exacerbations at baseline, and 0.99 for patients aged 65 years or older. Rates of exacerbations for subgroups with a history

Table 2 Proportion of patients with exact	erbations and number of exa	kacerbations in Year 2 (follow-up period)
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Variable	COPD patients with bronchitis receiving maintenance medications (n = 8554)	One or more exacerbations at baseline (n = 6298)	Two or more exacerbations at baseline (n = 3242)	Aged 65 years or older (n = 6759)
Sample with any exacerbation	4259 (49.8)	3620 (57.5)	2284 (70.5)	3277 (48.5)
[n (% of column)]				
Sample with severe exacerbations only	1188 (13.9)	993 (15.8)	602 (18.6)	946 (14.0)
[n (% of column)]				
Sample with moderate exacerbations only	2491 (29.1)	2091 (33.2)	1275 (39.3)	1903 (28.2)
[n (% of column)]				
Sample with both severe and	580 (6.8)	536 (8.5)	407 (12.6)	438 (6.5)
moderate exacerbations [n (% of column)]				
Exacerbation rate per patient per ye	ar [mean (SD)]			
Rate of any exacerbation	1.04 (1.51)	1.26 (1.64)*	1.77 (1.90)*	0.99 (1.46)
Rate of severe exacerbations	0.33 (0.84)	0.40 (0.93)*	0.56 (1.12)*	0.32 (0.81)
Rate of moderate exacerbations	0.70 (1.31)	0.86 (1.44)*	1.21 (1.74)*	0.67 (1.26)

Note: *Significantly different from overall COPD patients with bronchitis on maintenance medications, using the Wilcoxon rank-sum test (P < 0.05).

Abbreviations: COPD, chronic obstructive pulmonary disease; SD, standard deviation.

of exacerbations at baseline were significantly different from the overall population (P < 0.05, Table 2).

In line with the observed numbers of filled prescriptions reported in Table 1, annual COPD-related utilization in the overall population reported in Table 3 was dominated by pharmacy claims (91.6%), which were closely followed by physician office visits (75.8%). Approximately one-fifth of the cohort (20.6%) had COPD-related inpatient hospitalizations, and 13.9% had emergency room visits during the study time period. As expected, patients with two or more exacerbations dominated consumption in all utilization categories.

Patients with two or more exacerbations also led COPDrelated unadjusted annual costs (Table 3). Specifically, inpatient costs for the subgroup were almost double that for the overall population (\$2835 versus \$1576). Total COPDrelated annual costs were \$6381 for the subgroup with a history of two or more exacerbations, versus \$4069 for the overall population.

Patients who experienced both severe and moderate exacerbations led in adjusted COPD-related costs and in total health care cost per year (Table 4). After adjustment, total COPD-related costs were similar to unadjusted total costs for each of the one or more exacerbation and two or more exacerbation subgroups and for the group aged 65 years or older. COPD-related health care costs were substantially higher for all three groups than for the no exacerbation group (\$4875, \$6550, \$4050, versus \$1425, respectively), with a similar trend observed for total health care costs (\$20,418, \$23,346, \$18,038 versus \$11,747, respectively).

 Table 3 Annual chronic obstructive pulmonary disease (COPD)-related utilization and costs for COPD patients on maintenance medications

Variable	Overall COPD patients on maintenance	One or more exacerbations at baseline (n = 6298)	Two or more exacerbations at baseline (n = 3242)	Aged 65 years or older (n = 6759)		
	medications (n = 8554)					
Utilization per patient [mean (SD; % of patients)]					
Inpatient hospitalizations	1.2 (4.0; 20.6)	1.5 (4.4; 24.2)	2.2 (5.5; 31.0)	1.1 (3.6; 20.3)		
ER visits	0.2 (0.7; 13.9)	0.3 (0.8; 16.7)	0.4 (1.0; 22.0)	0.2 (0.7; 13.2)		
Physician office visits	7.9 (10.1; 75.8)	9.4 (10.8; 80.7)	12.4 (11.8; 89.0)	7.6 (9.9; 75.7)		
Pharmacy claims	9.7 (7.4; 91.6)	10.5 (7.7; 93.0)	12.2 (8.3; 96.4)	9.6 (7.3; 91.4)		
Costs per patient [mean (SD)]	a					
Inpatient hospitalizations	\$1576 (\$7578)	\$1903 (\$8330)	\$2835 (\$10,954)	\$1396 (\$5407)		
ER visits	\$87 (\$367)	\$108 (\$414)	\$158 (\$524)	\$78 (\$324)		
Physician office visits	\$1121 (\$1865)	\$1334 (\$2011)	\$1785 (\$2316)	\$1070 (\$1816)		
Pharmacy claims	\$1401 (\$1465)	\$1479 (\$1475)	\$1663 (\$1564)	\$1393 (\$1438)		
Total COPD-related costs	\$4069 (\$8635)	\$4720 (\$9430)	\$6381 (\$12,092)	\$3817 (\$6478)		

Note: "All figures given in US dollars.

Abbreviations: ER, emergency room; SD, standard deviation.

Table 4 Adjusted annual chronic obstructive pulmonary disease (COPD)-related and total health care costs^a in follow-up year

Variable	Adjusted mean COPD-related annual cost (95% CI)	Total health care cost per year (95% Cl)	
Patients with severe exacerbations only	\$12,765 (\$12,483-\$13,047)	\$43,042 (\$42,404-\$43,681)	
Patients with moderate exacerbations only	\$3356 (\$3293–\$3419)	\$14,188 (\$14,025-\$14,351)	
Patients with both severe and moderate exacerbations	\$14,721 (\$14,164–\$15,279)	\$43,385 (\$42,103-\$44,668)	
Patients with any exacerbations ^b	\$7022 (\$6926-\$7119)	\$25,894 (\$25,625-\$26,163)	
Patients with no exacerbations ^c	\$1425 (\$1404-\$1447)	\$11,747 (\$11,639–\$11,854)	
Patients with a history of one or more exacerbations ^d	\$4875 (\$4803–\$4946)	\$20,418 (\$20,225-\$20,611)	
Patients with a history of two or more exacerbations ^e	\$6550 (\$6451–\$6650)	\$23,346 (\$23,069-\$23,622)	
Patients aged 65 years or older	\$4050 (\$3986–\$4114)	\$18,038 (\$17,866-\$18,211)	

Notes: *All figures given in US dollars; ^bpatients with any exacerbations were patients with one or more severe and/or moderate exacerbations during the follow-up year; ^cpatients with no exacerbations were patients who had no severe or moderate exacerbations during the follow-up year; ^dpatients with a history of one or more exacerbations were patients who had one or more severe and/or moderate exacerbations during the baseline year – the reported mean costs shown were COPD-related annual costs during the follow-up year for this subgroup of patients; ^epatients with a history of two or more exacerbations were patients who had two or more severe and/or moderate exacerbations during the baseline year – the reported mean costs shown were COPD-related annual costs during the follow-up year for this subgroup of patients (note, this group is a subset of patients with a history of one or more exacerbations).

Abbreviation: CI, confidence interval.

Factors associated with the annual cost of exacerbation are provided in Table 5. Notably, experiencing a moderate or severe exacerbation was associated with incrementally higher cost than the cohort with no exacerbation. Exponentiation of the coefficients from the GLM suggested that, all else being equal, the cost ratio for a patient with a severe exacerbation relative to a patient with no exacerbations was 2.7, and for a patient with a moderate exacerbation versus a patient with no exacerbations the cost ratio was 1.17. Long-term

 Table 5
 Factors associated with annual cost of exacerbation

 by type

Variable	Coefficient	<i>P</i> -value (95% CI)
	estimate	
Age	-0.0072	<0.0001 (-0.0098 to -0.0046)
Race/ethnicity (versus wh	iite)	
Other	0.0772	0.0114 (0.0174–0.1371)
Hispanic	0.0930	0.0763 (-0.0098-0.1959)
Black	0.2250	<0.0001 (0.1372-0.3128)
Income	0.0719	0.0086 (0.0183-0.1256)
(high versus not high)ª		
Comorbidity		
CVD	0.5265	<0.0001 (0.4714–0.5816)
(versus no CVD)		
Diabetes	0.3765	<0.0001 (0.3208–0.4323)
(versus no diabetes)		
Maintenance medications		
ICS + LABA	0.1031	0.0005 (0.0452-0.1611)
LAMA	0.0939	0.0005 (0.0413-0.1465)
LABA	0.1361	0.0085 (0.0347-0.2376)
Long-term oxygen use	0.2164	<0.0001 (0.1691–0.2636)
Severe exacerbation	0.9925	<0.0001 (0.9285-1.0566)
Moderate exacerbation	0.1567	<0.0001 (0.0995-0.2139)

Note: ^aHigh income was defined by income \geq \$52,480 (in US dollars) (see Table 1). **Abbreviations:** CI, confidence interval of coefficient estimate; CVD, cardiovascular disease; ICS, inhaled glucocorticosteroid; LABA, long-acting β 2-agonist; LAMA, long-acting muscarinic antagonist. oxygen use, a proxy for severe disease, was associated with a cost ratio of 1.24. Each of the maintenance medications was also associated with higher health care costs, but coefficients were smaller than for long-term oxygen use. Cardiovascular disease was associated with a cost ratio of 1.69, and diabetes with a cost ratio of 1.46. The parameter estimate for age was close to zero (but negative), and statistically significant. This was an unexpected result, but it may reflect the fact that costs for commercial health plan members are higher than for Medicare members.

Discussion

The impact of the severity and frequency of exacerbations in patients with COPD can affect a patient's quality of life and can have long-term health consequences.^{1,5,24} The intensity and repetition of these episodes also affects health care costs for the patient, as well as for society in general because of the distribution of a number of health-related costs.^{25,26} Currently, there is a dearth of information available about COPD patients with chronic bronchitis. The majority of published studies examine COPD in general but do not address subgroups or the use of maintenance medications as the authors have done in the current study. In this study, the authors examined the health care utilization and costs associated with COPD patients with chronic bronchitis who experienced a range of moderate to severe exacerbations over a 12-month period.

In resource use and cost, relative to other subgroups, patients with two or more exacerbations led in every category, including rate of COPD exacerbations, physician office visits, and COPD-related and total health care costs. These results suggest that the more severe the disease, the greater the utilization and costs incurred by the patient. In fact, reduction of two or more exacerbations to none, based on the dollar amount reported here, could save \$5125 per patient per year in COPD-related health care costs and \$11,599 per patient per year in total health care costs (Table 4). Furthermore, preventing any exacerbations in patients with both severe and moderate exacerbations would save \$13,296 per patient per year, and simply reducing the severity of exacerbations from severe to moderate could save \$9409 per patient per year (Table 4). Factors associated with higher total health care costs extended beyond COPD to comorbidities such as cardiovascular disease and/or diabetes as well (Table 5). The exponentiated coefficients (1.69 for cardiovascular disease and 1.46 for diabetes) imply that these comorbidities add to health care costs by less than having a severe COPD exacerbation but by more than having a moderate COPD exacerbation, and are significant. The financial impact of these results is particularly significant in this vulnerable population largely made up of elderly patients enrolled in Medicare.

These results are similar to those reported by previous studies. For example, Yu et al²¹ observed that health care costs increased in parallel with the severity of exacerbations experienced by COPD patients. Similarly, as seen in the current study, Yu and colleagues²¹ demonstrated that all-cause costs were double for patients with any exacerbation compared with those without any exacerbation. However, although similar trends in data were observed in both the study by Yu et al²¹ and the current study, the cost and utilization rates reported by Yu et al²¹ were lower than those observed in the current study. This may be because Yu et al²¹ reported the data quarterly as opposed to annually, or it may be because Yu et al²¹ focused on the general COPD patient rather than restricting the study to COPD patients with chronic bronchitis. Also, the difference in data sources and/or geographic location of the members observed in both Yu et al's²¹ study and the current study may be other contributing factors to cost differences.

Notably, as with the study by Yu et al,²¹ the research reported in the current study was based on data from a claims database. One of the limitations inherent in using claims data is that clinical measures, such as FEV_1 , were not available to identify baseline severity of patients or to measure outcomes during follow-up. In addition, as with all claims data analyses, there is the possibility for error due to missing information that was not coded in the database. However, the use of a claims database does provide a range and depth of data not necessarily available from other resources. Importantly, studies examining the cost of COPD exacerbations in other countries (eg, France [this study included FEV₁ measures],²⁷ Canada,²⁸ and Poland²⁹) indicated that costs increased markedly with the severity of exacerbations, consistent with the current study.

A further limitation of the current study is that multivariate regression modeling was used to reduce selection bias and strengthen the causal inference. This type of modeling can only reduce bias caused by measured covariates; it cannot reduce bias caused by unmeasured covariates. Consequently, no causal inference can be ascertained from the current study.

Conclusion

Despite treatment with maintenance medications, COPD patients continue to have exacerbations resulting in high health care costs. Reduction of the severity and frequency of exacerbations can not only provide relief and clinical benefit to patients but also reduce the cost impact of the disease.³⁰ This has been demonstrated in research studies where reduction of exacerbations relates directly to the reduction of cost of care for the patient.¹¹ In fact, the largest potential for cost savings has been suggested to be in patients who have the highest rate of exacerbations that lead to expensive hospitalizations.¹¹ This reflects the observation reported in the current study that patients with more exacerbations incur significantly higher cost. The development of new medications and disease management interventions are clearly needed to further prevent or reduce COPD exacerbations and to reduce the cost and suffering caused by this disease.

Acknowledgment

The authors would like to thank Mary E Costantino, PhD, for her contributions to developing the manuscript.

Disclosure

Margaret Pasquale, Heather Hartnett, and Stephen Stemkowski are employees of Competitive Health Analytics. Frank Song was an employee of Competitive Health Analytics at the time of this study. Shawn Sun is an employee of Forest Research Institute. Competitive Health Analytics received payment from Forest Research Institute to conduct the study and draft this manuscript.

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